REMARKS

Amendments to the specification

The specification is amended as requested by the Examiner to provide the address of the depository at which biological material was deposited. No new matter is introduced by the amendments.

Claim status and claim amendments

Claims 14 and 16-30 were pending in the present application. Claims 14 and 16-30 are rejected on arguments laid out in the Office Action mailed on May 17, 2010.

Claims 38 and 39 are added to provide specific protection for the *E. coli* strain deposited at the International Depository Authority of Canada (IDAC) on January 21, 2005 under accession number IDAC 210105-01. Exemplary support for new claims 38 and 39 is found in the disclosure on page 5, lines 6 to 9 of the specification. This amendment does not add new matter. Upon entrance of the present amendments, claims 14, 16-30, and 38-39 are pending and presented for examination.

Rejection under § 112, first paragraph

Claim 23 is rejected as allegedly failing to comply with the enablement requirement. Claim 23 is directed to a method in accordance with the invention wherein a specific F4+ strain is used. This specific strain was deposited under accession number IDAC 210105-01 at the International Depository Authority of Canada (IDAC) on January 21, 2005. Applicants submit herewith a statement under 37 CFR 1.808 by the Assignee as suggested by the Examiner on page 4 of the Office Action. Furthermore, the specification as originally filed identifies on page 10 the deposit by accession number, date of deposit, name of the depository, and the complete taxonomic description (*Escherichia coli*). The present amendments to the specification further adds the address of the depository. Applicants therefore respectfully submit that the deposit meets all of the criteria set forth in 37 CFR 1.801-1.809. Applicants respectfully submit that the mere

filing of this statement should not be viewed as an admission that such a deposit is required to comply with the enablement requirement.

Applicants therefore respectfully request that the Examiner withdraw the rejection.

Rejection under § 102 (b)

Claims 14, 16-19, 24-27, and 29-30 stand rejected for allegedly being anticipated by Olshenitsky et al. (US 6511661). The Examiner takes the position that Olshenitsky teaches the claimed methods for promoting weight gain (or growth) in an animal.

Applicants would like to remind the Examiner that the present claims relate to uses of an F4+ non-pathogenic *E. coli* strain to promote growth in an animal.

F4 (also called K88) fimbriae are long filamentous polymeric surface proteins of enterotoxigenic *Escherichia coli* (ETEC). The F4 fimbriae allow microorganisms to adhere to F4-specific receptors present on brush borders of villous enterocytes and consequently to colonize the small intestine. Such ETEC infections are responsible for diarrhea and mortality in neonatal and recently weaned pigs.

It is well documented that F4 (or K88) positive strains are specific to pigs. It is also well-known that F4+ strains cannot and have not been isolated from bovines or humans. In this context, Applicants would like to bring the Examiner's attention to Table 1, on page 149 of a paper by Moon (submitted herewith in an Information Disclosure Statement), which confirms that the antigen type F known as F4 (or K88) is specifically associated with pigs. The host specificity of disease caused by K88+ ETEC is also discussed on page 153 of the same paper, where it is stated that the naturally occurring disease caused by K88+ ETEC is essentially confined to pigs. Humans are not susceptible to colonization by K88+ ETEC, even following experimental challenge.

Colonization factor antigens of human pathogens are also discussed in a paper by Evans *et al.* (submitted herewith in an Information Disclosure Statement). More

specifically, the article explains that K88 is a swine-associated ETEC. This article also emphasizes the need for specific intestinal epithelial cell receptors for ETEC colonization.

In particular, Applicants would like to bring the Examiner's attention to page 133, 2nd paragraph of the Evans article, where it is stated that:

> *The observed pattern of tissue affinity is in accord with the natural host of the ETEC isolates: K88-positive ETEC do not adhere to human intestine and do not cause diarrhea in man.* (Our emphasis)

In this context, Applicants respectfully note that the *E. coli* strains used in Olshenitsky were isolated from humans[1] and cannot therefore be F4+ *E. coli* strains since, as demonstrated above, F4+ *E. coli* strains cannot be obtained from human subjects. Besides, the *E. coli* strain used in Olshenitsky (i.e., ATCC deposit No. 202226 and DSM deposit No. 12799) was characterized as an F4– *E. coli* strain in later published PCT application WO 2007/136553 by Benson *et al.* (see Table 3 on page 10 of WO 2007/136553 which is submitted herewith in an Information Disclosure Statement). In particular, Applicants would like to bring the Examiner's attention to the last line of Table 3 which shows that the *E. coli* strain with ATCC deposit No. 202226 and DSM deposit No. 12799 is F4(K88) negative.

Therefore, contrary to what is concluded by the Examiner, the subject matter of claims 14, 16-19, 24-27, and 29-30 is clearly not anticipated by the disclosure of the *E.coli* F4– strains of Olshenitsky.

Applicants therefore respectfully request that the Examiner withdraw the rejection.

---

[1] As discussed in Example 2 of Olshenitsky (and also page 4, lines 28-29 of WO 2007/136553), the *E. coli* strain used in Olshenitsky (ATCC deposit No. 202226 and DSM deposit No. 12799) was "isolated from *E. coli* M17 by sequential transfer of isolates initiating from (2 months) survivors." The *E. coli* M17 strain is based on live culture of normal human microflora (see the first paragraph of the article by Chesnokova *et al.* which is submitted herewith in an Information Disclosure Statement).

Rejection under § 103(a)

Claims 14, 16-30 stand rejected for allegedly being obvious in view of Olshenitsky et al. (US 6511661). The Examiner has indicated that Olshenitsky teaches methods for promoting weight gain (or growth) in an animal comprising administering a non-pathogenic *E. coli* (abstract) in amounts to effect weight gain or animal growth.

The Examiner also states that the composition of Olshenitsky is fed orally as a feed or in a water carrier to post weaning animals such as day old calves, pigs and chickens.

As indicated above, the *E. coli* culture of Olshenitsky was isolated from the strain *E. coli* M-17 by sequential transfert of isolates initiating from long term (2 months) human survivors (see Example 2 of Olshenitsky). Therefore, all that is taught by Olshenitsky is the use of a formulation containing an F4– *E. coli* strain of human origin. Olshenitsky does not teach or suggest the use of a F4+ non-pathogenic *E. coli* strain as claimed.

As indicated earlier, an *E. coli* strain of human origin cannot be F4+ since the F4 receptor is only present in pigs and not in humans.

Applicants also respectfully note that Olshenitsky did not administer an F4+ *E. coli* culture as claimed in the instant application, but rather a formulation comprising the *E. coli* F4– probiotic culture and an aqueous solution of a volatile fraction prepared from the extract of at least one plant derived material (Examples 4 and 5). The growth promotion observed by Olshenitsky was not associated with the administration of an F4+ *E. coli* strain but with the vegetal volatile fraction included in the formulation as reported by Olshenitsky in different parts of the document (see column 4: line 18-22 and column 7: lines 50-57). The attribution of the growth promotion to the vegetal volatile fraction of the formulation was clearly stated in Example 13 (column 15) entitled *"Application of the Food/Feed Additive (Example 3) for the accelerated weight increase in healthy pigs"*. In this example and as shown below, the growth promotion was clearly associated with the

vegetal volatile fraction since the formulation used (Example 3) did not contain the *E. coli* strain.

> *Example 3: Preparation of food/feed additive formulation for the accelerated increase of body weight in mammals and avians:*
>
> *The mixture contained volatile fractions of: Alfalfa-50ml/liter, soy beans-200 ml/liter, beet-25 ml/liter and dill-100 ml/liter, prepared as described under Example 1 above. The balance was made up by distilled water.*

Furthermore, it was clearly reported that the F4– *E. coli* strain used by Olshenitsky was only responsible for prevention or treatment of different disorders as reported in different parts of the document (see column 4: lines 48-57, column 8: lines 1-3, column 8: lines 38-48, and column 9: lines 1-4).

Therefore, all examples of the Olshenitsky using the formulation comprising an F4– *E. coli* culture and a vegetal volatile fraction, and referred to by the Examiner, demonstrate that the F4– *E. coli* culture contained in the formulation has only a preventive and/or curative effect on diarrhea.

In view of the above, the subject matter of the claims presently on file is not obvious in view of the teaching of Olshenitsky. There is no teaching or suggestion in the Olshenitsky patent that would lead a person of skill in the art to the use of a non-pathogenic F4+ *E. coli* strain to promote growth in an animal.

Applicants therefore respectfully request that the Examiner withdraw the rejection of the claims for allegedly being obvious in view of Olshenitsky.

Conclusion

Applicants respectfully submit that the present case is now in condition for allowance. A Notice to that effect is requested. If a telephone conversation would help clarify any issues, or help expedite prosecution of this case, Applicants invite the Examiner to contact the undersigned at (617) 248-4793. Please charge any fees that may be required, or credit any overpayment, to our Deposit Account No. 03-1721, referencing Attorney Docket Number 2003390-0033.

Respectfully submitted,
CHOATE, HALL & STEWART LLP

Date: October 15, 2010

/Charles E. Lyon/
Charles E. Lyon, D.Phil.
Attorney for Applicant
Reg. No. 56,630

PATENT GROUP
CHOATE, HALL & STEWART LLP
Two International Place
Boston, MA 02110
Tel: (617) 248-4793
Fax: (617) 502-5002
clyon@choate.com